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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/556,938	02/23/2007	Chunyan Song	EX04-037C-US	7049

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MCDONNELL BOEHNEN HULBERT @ BERGHOFF LLP
300 SOUTH WACKER DRIVE
SUITE 3100
CHICAGO, IL 60606

EXAMINER	
SCHNIZER, RICHARD A	
ART UNIT	PAPER NUMBER
1635	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/556,938	SONG ET AL.	
	Examiner	Art Unit	
	Richard Schnizer	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 September 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-10* is/are pending in the application.

4a) Of the above claim(s) *4,5,and 7* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,6 and 8-10* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☒ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

An amendment was received and entered on 9/1/10.

Claims 13-15, and 20-25 were canceled.

Claims 1-10, remain pending.

Claims 4, 5, and 7 stand withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 5/13/09

Claims 1-3, 6, and 8-10 are under consideration in this Office Action.

Oath/Declaration

The Oath/Declaration stands objected to for the reasons of record. Applicant's indication that a new Oath/Declaration will be submitted is acknowledged.

Claim Rejections - 35 USC § 103

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 1-3, 6, 8, and 9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Forler et al (Mol. Cell. Biol. 24(3): 1155-1167, 2/204) in view of Yokoyama et al (Nature 376: 184-188, 1995) as evidenced by Shin et al (Cancer Lett. 287: 231-239, 2010), Yu et al (EMBO J. 28:21-33, 2009), Honegger et al (J. Biol. Chem. 261(2): 569-575, 1986), Zhou et al (Gyn. Oncol. 101:305-310, 2006), Wetterau et al (J.

Clin. Endocrinol. Metab. 88(7): 3354-3359, 2003), and Tao et al (FEBS Letters 454: 312-316, 1999).

Forler inhibited expression of RANBP2 in Drosophila S2 cells by RNA interference and showed that this resulted in complete inhibition of cell proliferation. See Fig. 1(f).

Forler did not teach inhibition of any of SEQ ID NOS: 1-6.

Yokoyama studied the structure and function of human RANBP2, using cultured human (HeLa) cells. It would have been obvious to one of ordinary skill in the art at the time of the invention to extend the studies of Forler to human cells, such as the HeLa cells of Yokoyama, because the function of RANBP2 in human cells was clearly of interest, as evidenced by Yokoyama. Absent evidence to the contrary, the HeLa cells of Yokoyama encode RANBP2 of SEQ ID NO: 1, i.e. they are wild type for RANBP2. Accordingly, it would have been obvious to one of ordinary skill in the art at the time of the invention to inhibit expression of RANBP2 in the cells of Yokoyama using an RNA interference molecule comprising an antisense oligomer, essentially as taught by Forler. This would require developing an RNAi agent specific for human RANBP2. It would have been obvious to first test different RNAi agents in order to select one that functioned well to decrease RANBP2 expression in HeLa cells, thus rendering obvious steps a-c of the claims.

It then would have been obvious to use the selected RNAi agent to examine in detail the effects of RANBP2 inhibition on cellular proliferation in the HeLa cells of Yokoyama in order to determine if the same effects were observed as in the S2 cells of

Forler. Note that HeLa cells comprise active IGF receptors and active PTEN as evidenced by Shin (page 235, section 3.6) and Yu et al at page 24, left column, first full paragraph). Moreover it was clear from Shin that HeLa cells are cultured in media containing fetal bovine serum (see page 233, section 2.2), which inherently contains IGF-1 (see Honegger, abstract). Thus, it would have been obvious to assay cellular proliferation of the HeLa cells in the presence of IGF-1. Absent evidence to the contrary, the measurement of changes in cellular proliferation would serve as a measurement of changes in IGF/PTEN signaling, and the invention as a whole was prima facie obvious.

Claim 3 is included in this rejection because it is known in the art that HeLa cells overexpress telomerase (See Tao, abstract, and paragraph bridging columns on page 312), and that telomerase expression is modulated by PTEN (see Zhou, abstract) and by IGF (see Wetterau, abstract). Accordingly telomerase expression is a function of the PTEN/IGF pathway, and HeLa cells are considered to have defective PTEN/IGF function because they have inappropriate telomerase expression. The office does not have the facilities for examining and comparing Applicant's product with the product of the prior art in order to establish that the product of the prior art does not possess the same material, structural and functional characteristics of the claimed product. In the absence of evidence to the contrary, the burden is upon the applicant to prove that the claimed products are functionally different than those taught by the prior art and to establish patentable differences. See Ex parte Phillips, 28 USPQ 1302, 1303 (BPAI 1993), In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and Ex parte Gray, 10

USPQ2d 1922, 1923 (BPAI 1989), and MPEP 2112(V), 2112.01(I), and 2112.02. It is noted that the instant claims are not product claims, but the issue here is whether or not a recited product (cultured cells with defective PTEN/IGF function) are equivalent to the a prior art product (HeLa cells with defective control of telomerase expression).

Claim 10 is are rejected under 35 U.S.C. 103(a) as being unpatentable over Forler et al (Mol. Cell. Biol. 24(3): 1155-1167, 2/2004) and Yokoyama et al (Nature 376: 184-188, 1995) as applied to claims 1, 2, 3, 6, 8, and 9 above and further in view of Sokoloff et al (US 7071163).

The teachings of Forler and Yokoyama render obvious a method of identifying in HeLa cells an RNAi agent that inhibits RANBP2, and then assaying the effect of that agent on cellular proliferation in the presence of IGF-1.

These references did not teach a PMO.

Sokoloff taught that interfering RNA and morpholino antisense nucleic acids were functional alternatives as expression inhibitors (paragraph bridging columns 12 and 13), and taught that synthetic oligomers could contain phosphorodiamidate backbones (column 11, lines 36-39).

It would have been obvious to one of ordinary skill in the art at the time of the invention use an antisense PMO oligomer in the method rendered obvious by Forler and Yokoyama because Sokoloff taught that gene expression could be inhibited by alternative means including RNA interference and antisense oligonucleotides. In view of the teachings of Sokoloff, it was routine in the art to modify antisense oligomers,

either as siRNA strands or more classical antisense agents, with PMO linkages. One would have been motivated to make such modification in order to improve the stability of the oligomer. Thus the invention as a whole was prima facie obvious.

Response to Arguments

Applicant's arguments filed 9/1/10 have been fully considered but they are not persuasive.

Applicant asserts that Forler is not appropriate prior art because Forler was published in February 2004 whereas the instant application claims priority to provisional application 60/470766, filed 5/14/2003. This is unpersuasive because 60/470766 fails to provide adequate support or enablement in the manner provided by the first paragraph of 35 U.S.C. 112 for the instant claims, and therefore the instant claims are not entitled to a filing date of 5/14/2003. For example, all instant claims read on methods of detecting instant SEQ ID NOS: 2-6, *e.g.* by nucleotide sequence or as a molecule consisting of SEQ ID NO: 2, 3, 4, 5, or 6. However, while 60/470766 disclosed a sequence that is identical to instant SEQ ID NO: 1, none of SEQ ID NOS: 2-6 is disclosed in 60/470766 as an independent sequence, and none of SEQ ID NOS: 2, 3, 5, or 6 is disclosed as a complete sequence within the disclosed sequence (SEQ ID NO: 1). As a result, 60/470766 does not provide adequate support in the manner provided for by the first paragraph of 35 USC 112, and the effective filing date of the instant claims is 5/13/2004, the filing date of PCT/US2004/015145. Accordingly, the Forler reference is available as prior art under 35 USC 103(a).

Applicant argues at page 6 of the response, first and second paragraphs, that Yokoyama fails to teach or suggest the claimed method steps. This is unpersuasive because Forler taught inhibition of RANBP2 expression in Drosophila S2 cells by RNA interference and showed that this resulted in complete inhibition of cell proliferation, and as outlined in the rejection above, it would have been obvious to one of ordinary skill in the art at the time of the invention to extend the studies of Forler to human cells, such as the HeLa cells of Yokoyama. This is because the function of RANBP2 in human cells was clearly of interest, as evidenced by Yokoyama. In doing so, the instant method steps would have been obvious for the reasons set forth in the rejection.

Applicant asserts that Yokoyama fails to recognize the connection between RANBP2 and PTEN. However, Applicant is reminded that the reason or motivation to modify cited references may often suggest what the inventor has done, but for a different purpose or to solve a different problem. Thus knowledge of a relationship between RNABP2 and PTEN is not necessary to render obvious the claimed invention if it was obvious to perform the active method steps for any reason. Such a reason is set forth in the rejection. The remainder of Applicant's arguments are based on the position that the Forler reference is not available as prior art and that the remaining references fail to teach the claimed method steps. This is unpersuasive because Forler is available as prior art, as discussed above. For these reasons the rejections are maintained.

Conclusion

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner(s) should be directed to Richard Schnizer, whose telephone number is 571-272-0762. The examiner can normally be reached Monday through Friday between the hours of 6:00 AM and 3:30 PM. The examiner is off on alternate Fridays, but is sometimes in the office anyway.

If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, Christopher Low, can be reached at (571) 272-0951. The official central fax number is 571-273-8300. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Richard Schnizer/
Primary Examiner, Art Unit 1635